361 ENDOGENOUS ANGIOTENSIN STIMULATION OF VASOPRESSIN (AVP) IN THE NEWBORN LAMB.

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Exogenous renin or angiotensin II (A II) infused peripherally or into the CNS will stimulate thirst and AVP release. Whether the endogenous renin-angiotensin system physiologically stimulates thirst or AVP secretion is unknown. To assess the effect of endogenous renin-angiotensin stimulation on AVP secretion in the lamb, nine normal newborn lambs were stimulated with furosemide (FU) 2 mg/kg infused I.V. alone, and with the A II inhibitor 1-sar, 8-ala, A II, 5 μg/kg/min. Six anephric lambs received only FU. Blood samples were drawn at 8, 20, 35, 65 and 125 min. post infusion. PRA (ng/ml/hr), aldosterone (aldo, ng/dl) and AVP (μU/ml) were measured by RIA. (M and SEM) PRA increased within 8 min. from a baseline of 16.7±5.0 to 30.2±12.3 ($p<.05$), and remained elevated through 120 min. Plasma Aldo and AVP increased post FU from respective baselines of 14.2±4.7 and 2.7±0.5, to 28.5±13.2 and 9.9±3.5 at 35 min. ($p<.05$), and thirst-like behavior was observed. AVP, thirst, and Aldo did not increase after FU in anephric lambs or in normal lambs treated with A II inhibitor. There were no changes in mean plasma sodium, Hct, or osmolality, and minimal changes in systemic blood pressure and plasma protein concentration during the first 35 min. after FU.

We conclude: 1) that FU stimulates Aldo, AVP and thirst via direct renal stimulation of renin, 2) the Aldo, AVP and thirst responses to FU are mediated by A II release and 3) these responses all are intact in the newborn period.

362 CATECHOLAMINE EXCESS IN THE NEWBORN: A NEW SYNDROME.

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We measured strikingly increased urinary and serum levels of catecholamines in a newborn with gangrene of the extremities, hypertension (BP 200/160), myocarditis, enterocolitis, hematologic abnormalities (thrombocytopenia, hyperkininemia with edema, disseminated intravascular coagulation) renal disease (proteinuria, oliguria), seizures and coma. Total serum catechols were 6.0 ng/ml (normal 0.2-0.5 ng/ml). Urine catechol levels in ug/mg creatinine were determined before and after 12 hrs. of therapy with α-methyl-paratyrosine (α-MPT), an inhibitor of endogenous catechol synthesis.

	VMA	HVA	Met+NMET
Pre α -MPT	20	8	14.4
12 hrs. of α -MPT	5	6	16.3
Normal & (SD)	6.9(3.2)	12.9(9.5)	1.64(1.32)

Phentolamine test was positive; treatment with peripheral alpha-blockade normalized blood pressure. During one month of α-MPT therapy, all chemical and physical abnormalities were largely reversed. Two attempts to taper α-MPT were followed by hypertension. Following death attributable to sepsis and DIC, extensive autopsy failed to reveal a catechol source. Because catechol excess is a potentially treatable cause of this catastrophic circulatory disorder, it should be considered in the differential diagnosis of hypertension and of peripheral gangrene in infants.

363 ALPHA GLYCOPROTEIN HORMONE SUBUNIT (α) AFTER LRF IN UNTREATED AND ESTROGEN TREATED GONADAL DYSGENESIS.

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Glycoprotein hormones share a common α subunit but each has a β subunit which confers biologic and immunologic specificity. Elevated plasma LH and FSH in hypergonadotropic hypogonadism can be lowered by estrogen therapy, but the change in circulating plasma α with therapy is undefined. We administered 100 μg LRF IV to 7 normal girls 12-18 yrs (Norm) and to 7 patients 12-20 yrs with gonadal dysgenesis (GD) before and during (GD-RX) 9 months of 0.3 mg/day of oral conjugated estrogens and found:

	α: basal	α: peak	LH: basal	LH: peak	FSH: basal	FSH: peak
GD	4.2	18.9	9.3	43.4	46.7	78.0
	Δ	†	*	Δ	*	†
GD-RX	1.3	5.1	3.3	11.8	17.8	23.3
Norm	.8	3.7	1.4	6.4	1.6	3.6

(*=$p<.02$; †=$p<.01$; Δ=$p<.0001$) (in ng/ml by radioimmunoassay)

The cross reaction (<10%) of LH or FSH in the α radioimmunoassay did not account for the α levels. A difference in time of peak α levels was seen in GD and GD-RX compared to normal. In conclusion: 1) Basal and LRF stimulated α are significantly higher in GD than normal girls but low dose estrogen therapy lowers α levels to normal. 2) α is released from the pituitary independently of LH or FSH. 3) Estrogen lowers basal LH and FSH in GD-RX and decreases the gonadotropin hyperresponse to LRF.

364 DEXAMETHASONE AND ITS EFFECT ON ADRENAL FUNCTION IN PREMATURES.

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Fourteen pregnant patients at 26-33 weeks of gestation received up to 6 doses of either 4 mg dexamethasone phosphate or placebo intramuscularly. All were delivered within 12 hours of the last dose. The mean (±SE) birth weight and gestational age of the treated group of 1405±33 gm and 31.0±1.1 weeks was not different ($p>0.05$) from that of the nontreated group (1600±230 gm and 30.4±0.9 weeks). Maternal and umbilical venous blood samples were obtained at delivery, and the concentration of dehydroepiandrosterone sulfate (DS), cortisol (F), cortisone (E), and dexamethasone (Dexa) was measured by radioimmunoassay with the following results (expressed as μg/100 ml):

	Maternal Venous				Umbilical Venous			
	DS	F	E	Dexa	DS	F	E	Dexa
Term	--	33.6	4.0	--	--	4.8	8.9	--
Placebo	213	44.6	6.3	--	248	5.5	10.0	--
Dexa	55	15.1	---	9.1	112	1.5	4.1	7.6

These data indicate that at 26-33 weeks of gestation, dexamethasone will readily cross the placenta and suppress fetal adrenal function. Umbilical venous cortisol and cortisone levels at 26-33 weeks are comparable to those found in term pregnancy and the degree of fetal adrenal suppression following multiple doses of dexamethasone is similar to that seen following a single 4 mg dose of dexamethasone given at term pregnancy.

365 THYROID FUNCTION IN INFANTS ADMITTED TO A NEONATAL INTENSIVE CARE UNIT (NICU): A LONGITUDINAL ASSESSMENT.

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Serum thyroxin values (T_4) were found to be low in 6 of 1350 admissions when the tests were ordered on clinical grounds. Hypothyroidism was confirmed in 3 infants, but the remaining 3 had transient depressions of T_4 due to binding globulin (TBG) deficiency. Consequently, a longitudinal study was carried out on 9 infants (gestation 30-34 wks). Data are means ± SE.

	cord	24 h	72 h	1 week	2 weeks	3 weeks
n	3	8	8	8	9	9
T_4 ug/dl	4.7±1.2	7.3±0.9	6.4±1.2	8.4±1.9	7.7±1.2	8.9±0.7
Range	3.2-7.0	5.6-11.7	2.9-12.6	1.6-17.4	3.6-15.8	7.1-13.2
TSH uU/ml	8.9±1.5	8.8±1.9	4.1±0.7	3.4±0.3	3.5±0.3	3.8±0.4
Range	6.8-11.8	3.0-16.9	3.0-7.4	3.0-4.5	3.0-6.1	3.0-6.9

($p<0.05$ for cord and 24h TSH vs. TSH at 72h-3wks)

Four infants displayed a transient decline in T_4 levels (≥40% of their 24h value) at some time between 72 hrs and 2 wks, a pattern unlike the normal full-term baby. These data indicate that for infants admitted to a NICU: 1. The incidence of hypothyroidism may be higher than in the general population; 2. T_4 values vary markedly and falsely low values may occur frequently; 3. A TSH determination on or after 72 hours of life may be the most appropriate screen for hypothyroidism; 4. Transient decrements in T_4 may reflect a transient TBG deficiency.

366 GLUCAGON RESPONSES IN ARGININE-INSULIN TOLERANCE TESTS IN GROWTH HORMONE DEFICIENCY.

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Twelve children were studied with arginine-insulin tolerance tests (AITT). Nine were growth hormone (GH) deficient; three of these had TSH deficiency and were studied after full thyroid hormone replacement. No child was found to have ACTH deficiency. Subjects were divided into three groups based on GH response and hypoglycemic symptomatology. Group I: normal responders with mild symptoms (tachycardia, diaphoresis). Group II: GH deficient children with mild symptoms. Group III: GH deficient children with cerebral symptoms requiring IV glucose.

Glucose, cortisol, and insulin levels were comparable in all subjects. GH secretion was negligible in all GH deficient subjects. The glucagon and glucose responses were: (mean ± SEM)

Group	N	mean glucose nadir (mg/dl)	Glucagon Levels (pg/ml) mean basal	mean peak
I (Normals)	3	29 ± 9	186 ± 34	998 ± 260 *
II (GH Def)	6	30 ± 3	342 ± 98	1334 ± 308 *
III (GH Def)	3	27 ± 3	188 ± 34	490 ± 250

* Significant at $p < .05$ in comparison with Group III

These data suggest an association between glucagon secretion during the AITT and the degree of hypoglycemic symptomatology. Glucagon in high plasma concentration may retard the development of the cerebrally mediated hypoglycemic symptoms despite low plasma glucose levels.

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